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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/651,374 08/30/00 WITTWER

C A-68197/RFT/

EXAMINER

HM22/0716

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ART UNIT	PAPER NUMBER
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1656

DATE MAILED:

07/16/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/651,374

Applicant(s)
Wittwer et al.

Examiner
Joyce Tung

Art Unit
1656



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above, claim(s) 23-45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-22 is/are rejected.
- 7) ☒ Claim(s) 12-22 is/are objected to.
- 8) ☒ Claims 1-45 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 4
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other: _____

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DETAILED ACTION

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1656.

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:
 - I. Claims 1-22, drawn to a method of analyzing a nucleic acid sample comprising multiple loci by measuring fluorescence resonance energy transfer via hybridization, classified in class 435, subclass 6.
 - II. Claims 23-40, drawn to a method of analyzing a nucleic acid sample comprising multiple loci by measuring fluorescence resonance energy transfer via amplification, classified in class 435, subclass 91.2.
 - III. Claims 41-45, drawn to a device for multichannel color analysis of a target nucleic acid amplification reaction, classified in class 435, subclass 288.7.
2. The inventions are distinct, each from the other because of the following reasons:

Inventions I-III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions, Invention I, claims 1-22 involves hybridization, Invention II, claims 23-40 involves

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amplification and Invention III, claims 41-45 is drawn to a device for multichannel color analysis of a target nucleic acid amplification reaction.

3. Because these inventions are distinct for the reasons given above and the search required for Group is not required for Group , restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Mr. James J. Diehl on 4/6/2001 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-22. Affirmation of this election must be made by applicant in replying to this Office action. Claims 23-45 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper tames extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.d. 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-11 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 7-16 of U.S. Patent No. 6,197,520. Although the conflicting claims are not identical, they are not patentably distinct from each other because Claims 1-11 are drawn to a method of analyzing a nucleic acid sample comprising multiple loci in which a first locus has at least two possible allelic sequences and a second locus has at least three possible allelic sequences. The method of claims 1-11 comprises combining at least two pairs of oligonucleotide probes containing donor and acceptor fluorescein as listed in claims 10-11, measuring the emission of each of said FRET acceptors at a first temperature and repeating said emission measurements at a second and third temperature in which the measurements at different temperatures provide an indication of the alleles present at said first and second loci. The scope of claims 1-11 overlaps the scope of claims 7-16 of U.S. Patent No. 6,197,520 because the method of claims 7-16 are drawn to a method of analyzing the genotype of multiple loci of nucleic acid sequence involving the similar method steps as claimed in claims 1-11.

Claim Rejections - 35 U.S.C. § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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- a. Claims 1-11 are vague and indefinite because the language in step (a) of claim 1 is unclear whether or not the second pair of oligonucleotide probe is hybridized to the said second locus which is within the same segment in the nucleic acid sample as the first pair of oligonucleotide probe is hybridized. It is suggested to clarify uncertainty.
- b. Claims 1-11 are vague and indefinite because of the language “the second member of said second” in step (a) of claim 1. It is unclear what is involved in the second member. It is suggested to clarify uncertainty.
- c. Claims 1-41 are vague and indefinite because it is unclear how the differential hybridization is corresponding to the emission of said FRET acceptors at different temperatures which provide an indication of the alleles present at different loci (or multiples loci).
- d. Claims 4 and 15 are vague and indefinite because it is unclear what is a member of two different probe pairs.
- e. Claims 1-11 are vague and indefinite because it is unclear whether the first pair of oligonucleotide probe hybridizes to said first locus or hybridizes each other. It is suggested to clarify uncertainty.
- f. Claims 12-22 are vague and indefinite because of the language “each of the members of said pairs being capable of hybridizing in proximity to each other within a segment of said nucleic acid comprising at least one of said multiple loci”. It is unclear whether or not each of the members of said pairs hybridizes to each other. It is suggested to clarify uncertainty.

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Claim Rejections - 35 U.S.C. § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-3, and 5-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wittwer et al. (6,197,520).

Wittwer et al. disclose a method of detecting mutations and polymorphisms at multiple loci of a genomic DNA sample. The method involves two or more FRET oligonucleotide pairs, illuminating the sample with the appropriate wavelength, monitoring the fluorescence as a function of temperature during heating and compensating the fluorescent values (See column 5, lines 20-26). The genotypes of a nucleic acid sample at more than one locus is identified by measuring fluorescence throughout a range of temperature and correcting for temperature-

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dependent spectral overlap of the fluorescent probes (See the Abstract). The temperature range of analysis is between 40-95°C and the temperature ramp is a 0.2°C/S (See column 9, lines 24-30). The fluorescein dye is LC Red 705 and LC Red 640 (See column 16, lines 47-51).

Wittwer et al. do not disclose using a specific number of pairs for specific locus and three temperature measurements of fluorescence emission to analyze a nucleic acid sample as claimed.

The teachings of Wittwer et al. suggest the limitations of claims 1-3 and 5-11. Claims 1-3 and 5-11 are drawn to a method of analyzing a nucleic acid sample comprising multiple loci in which a first locus has at least two possible allelic sequences and a second locus has at least three possible allelic sequences. The method comprises combining at least two pairs of oligonucleotide probes containing donor and acceptor fluorescein as listed in claims 10-11. Each pair hybridizes to the locus in proximity within a segment of nucleic acid. One members of the first pair has a sequence which results in the differential hybridization of that member with at least two different alleles at first locus. Each of said FRET acceptors is measured at a first temperature and repeatedly measured at a second and third temperature. The temperature varies within a range between 20°C to 95°C at least 0.01 to 1°C per second. The emission measurements at a particular temperature are simultaneous.

One of ordinary skill in the art at the time of instant invention would have been motivated to apply the teachings of Wittwer et al. to make instant invention because of the teaching disclosed by Wittwer et al. (See column 15 to 16) as set forth above and the benefit of the invention of Wittwer et al. that the invention allows for a rapid procedure within a single reaction

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vessel for detecting mutations and polymorphisms at multiple loci using FRET pair of oligonucleotide probe at a desired temperature range (See column 5, lines 12-16). It would have been prima facie obvious to carry out the method as claimed.

Allowable Subject Matter

11. Claims 12-22 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

12. The following is a statement of reasons for the indication of allowable subject matter:

No prior art has been found teaching or suggesting a method of analyzing a nucleic acid sample comprising multiple loci using three pairs of oligonucleotide probes in which each of the second and third probe pair has a different T_m from each other for each different allele within the nucleic acid segment to which each member hybridizes. The analysis involves the emission measurement of FRET. The closest prior art is the reference of Wittwer et al.. The teachings of Wittwer et al. are set forth in section 10 above, but Wittwer et al. do not disclose the probe pair has a different T_m from each other for each different allele within the nucleic acid segment to which each member hybridizes.

13. Any inquiries concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (703) 305-7112. The examiner can normally be reached on Monday-Friday from 8:00 AM-4:30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached at (703) 308-1152.

Any inquiries of a general nature or relating to the status of this application should be directed to the Chemical/Matrix receptionist whose telephone number is (703) 308-0196.

14. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Art Unit 1656 via the PTO Fax Center located in Crystal Mall 1 using (703) 305-3014 or 308-4242. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Joyce Tung

July 15, 2001 